Amd. dated October 20, 2003
Reply to Office Action of May 23, 2003

## Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

### Listing of Claims:

Claims 1-125 (Cancelled).

126 (New). A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a 5,10,15-triaryl-corrole of the formula:

wherein  $Ar_1$ ,  $Ar_2$ , and  $Ar_3$ , the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$ 

alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$  alkylammonium radicals, and wherein at least two of said aryl radicals are positively charged, n is an integer from 2 to 3 and X is a pharmaceutically acceptable anion.

127 (New). The pharmaceutical composition according to claim 126, wherein said carboaryl radical is phenyl substituted by fluoro and optionally by  $tri-(C_1-C_8)$  alkylammonium or amino- $(C_1-C_8)$  alkylamino.

128 (New). The pharmaceutical composition according to claim 127, wherein one or two of said carboaryl radicals is pentafluorophenyl and/or 4-aminopropylamino-2,3,5,6-tetrafluorophenyl.

129 (New). The pharmaceutical composition according to claim 127, wherein one to three of said carboaryl radicals is 4-trimethylammoniophenyl or 4-trimethylammonio-2,3,5,6-tetrafluorophenyl.

 $130\,(\text{New})$  . The pharmaceutical composition according to claim 126, wherein one to three of said heteroaryl radicals is N-  $(C_1-C_8 \text{ alkyl})$ -pyridylium.

131 (New). The pharmaceutical composition according to claim 130, wherein said radical is selected from the group consisting of 2-, 3- and 4-(N-methyl) pyridylium.

132 (New). The pharmaceutical composition according to claim 126, wherein said mixed carboaryl-heteroaryl radical is 4-(N-methyl-2-pyridylium)-2,3,5,6-tetrafluorophenyl.

133 (New). The pharmaceutical composition according to claim 132, wherein the 5,10,15-triaryl-corrole is the compound 5,10,15-tris[2,3,5,6-tetrafluorophenyl-4- (N-methyl-2-pyridylium)]-21H,23H-corrole triiodide.

134 (New). A method for inhibiting growth factor receptor tyrosine kinase activity in a patient in need thereof, which comprises administering to said patient a tetrapyrrolic macrocycle selected from the group consisting of:

(a) a 5,10,15,20-tetraaryl-porphyrin of the formula:

wherein  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$ , the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ ) alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ ) alkylamino mium radicals, wherein at least two of said  $Ar_1$ ,  $Ar_2$ ,

Ar<sub>3</sub>, and Ar<sub>4</sub> aryl radicals are positively charged, n is an integer from 2 to 4 and X is a pharmaceutically acceptable anion, provided that at least two of said at least two positively charged Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub> aryl radicals are selected from the group consisting of N- $(C_1-C_8)$  alkyl-pyridylium, 4-tri $(C_1-C_8)$  alkyl-ammonium)-2,3,5,6-tetrafluorophenyl and 4-N- $(C_1-C_8)$  alkyl-pyridylium)-2,3,5,6-tetrafluorophenyl and, when at least two of said positively charged Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub> radicals are N- $(C_1-C_8)$  alkyl-pyridylium, at least one of the remaining Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub> is a non-positively charged aryl radical selected from the group consisting of pentafluorophenyl and 4-amino $(C_1-C_8)$  alkylamino-2,3,5,6-tetrafluorophenyl; and

(b) 5,10,15-triaryl-corrole of the formula:

wherein  $Ar_1$ ,  $Ar_2$ , and  $Ar_3$ , the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical,

wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$  alkylamino amino-ium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$  alkylammonium radicals, and wherein at least two of said aryl radicals are positively charged, n is an integer from 2 to 3 and X is a pharmaceutically acceptable anion;

in an amount sufficient to inhibit growth factor receptor tyrosine kinase activity.

135 (New). A method according to claim 134 which comprises administration of a 5,10,15,20-tetraaryl-porphyrin of the formula:

wherein Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub>, the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy,  $C_1-C_8$  alkylamino, amino- $(C_1-C_8)$  alkylamino, and tri- $(C_1-C_8)$ alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1\text{-}C_8$  alkyl,  $C_1\text{-}C_8$ alkoxy,  $C_1-C_8$  alkylamino, amino- $(C_1-C_8)$  alkylamino, and tri- $(C_1-C_8)$ alkylammonium radicals, wherein at least two of said Ar<sub>1</sub>, Ar<sub>2</sub>,  $Ar_3$ , and  $Ar_4$  aryl radicals are positively charged, n is an integer from 2 to 4 and X is a pharmaceutically acceptable anion, provided that at least two of said at least two positively charged Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub> aryl radicals are selected from the group consisting of  $N-(C_1-C_8)$  alkyl-pyridylium,  $4-tri(C_1-C_8)$  alkylammonium) -2, 3, 5, 6-tetrafluorophenyl and 4-N-( $C_1$ - $C_8$ ) alkylpyridylium) -2,3,5,6-tetrafluorophenyl and, when at least two of

said positively charged  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$  radicals are N- $(C_1-C_8)$  alkyl- pyridylium, at least one of the remaining  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$  is a non-positively charged aryl radical selected from the group consisting of pentafluorophenyl and 4-amino( $C_1-C_8$ ) alkylamino-2,3,5,6-tetrafluorophenyl, in an amount sufficient to inhibit said growth factor receptor tyrosine kinase activity.

136 (New). The method according to claim 135, wherein one or two of said carboaryl radicals is pentafluorophenyl and/or 4-aminopropylamino-2,3,5,6- tetrafluorophenyl.

137 (New). The method according to claim 135, wherein said carboaryl radical is phenyl substituted by fluoro and optionally by  $\text{tri-}(C_1-C_8)$  alkylammonium.

138 (New). The method according to claim 136, wherein one to two of said carboaryl radicals is 4-trimethylammonio-2,3,5,6- tetrafluorophenyl.

139 (New). The method according to claim 135, wherein said mixed carboaryl-heteroaryl radical is 4-(N-methyl-2-pyridylium)-2,3,5,6-tetrafluorophenyl.

140 (New). The method according to claim 135, wherein said 5,10,15,20-tetraaryl-porphyrin compound is selected from the

group consisting of the compounds herein designated P15, P16, P17, P18, P19 and P20, namely:

P15 5,10,15,20-tetrakis(2,3,5,6-tetrafluoro-4-trimethylammonio-phenyl)-21H, 23H-methyl-porphine tetratrifluoromethylsulfonate

P16 5-pentafluorophenyl-10,15,20-tris(N-methyl-4pyridylium)-21H, 23H-porphine triiodide

P17 5,15-bis(pentafluorophenyl)-10, 20-bis(N-methyl-4pyridylium)-21H, 23H- porphine diiodide

P18 5,10-bis(pentafluorophenyl)-15, 20-bis(N-methyl-4pyridylium)-21H, 23H- porphine diiodide

P19 5,10,15-tris(N-methyl-4-pyridylium)-20-(2,3,5,6-tetrafluoro-4-aminopropyl-amino-phenyl)-21H, 23H-porphine triiodide

P20 5,10,15,20-tetrakis[4-(N-methyl-2-pyridylium)
2,3,5,6-tetrafluoro-phenyl]-21H, 23H-porphine tetraiodide.

141(New). A method according to claim 134 activity which comprises administration of a 5,10,15-triaryl-corrole of the formula:

$$\begin{bmatrix} & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\$$

wherein Ar<sub>1</sub>, Ar<sub>2</sub>, and Ar<sub>3</sub>, the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy,  $C_1-C_8$  alkylamino, amino- $(C_1-C_8)$  alkylamino, and tri- $(C_1-C_8)$  alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1\text{-}C_8$  alkyl,  $C_1\text{-}C_8$ alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$ alkylammonium radicals, and wherein at least two of said aryl radicals are positively charged, n is an integer from 2 to 3 and

X is a pharmaceutically acceptable anion, in an amount sufficient to inhibit said growth factor receptor tyrosine kinase activity.

142 (New). The method according to claim 141, wherein said carboaryl radical is phenyl substituted by fluoro and optionally by  $\text{tri-}(C_1-C_8)$  alkylammonium or  $\text{amino-}(C_1-C_8)$  alkylamino.

143 (New). The method according to claim 141, wherein one or two of said carboaryl radicals is pentafluorophenyl and/or 4-aminopropylamino-2,3,5,6- tetrafluorophenyl.

144 (New). The method according to claim 142, wherein one to three of said carboaryl radicals is 4-trimethylammoniophenyl or 4-trimethylammonio-2,3,5,6-tetrafluorophenyl.

145 (New). The method according to claim 141, wherein said one to three of said heteroaryl radicals is  $N-(C_1-C_8 \ alkyl)$  - pyridylium.

146 (New). The method according to claim 145, wherein said radical is selected from the group consisting of 2-, 3- and 4-(N-methyl) pyridylium.

147 (New). The method according to claim 141, wherein said mixed carboaryl-heteroaryl radical is 4-(N-methyl-2-pyridylium)-2,3,5,6-tetrafluorophenyl.

148 (New). The method according to claim 141 wherein the 5,10,15-triaryl-corrole is 5,10,15-tris[2,3,5,6-tetrafluorophenyl-4-(N-methyl-2-pyridylium)]-21H,23H-corrole triiodide.

149 (New). The method according to claim 134, wherein said growth factor receptor tyrosine kinase is selected from the group consisting of fibroblast growth factor (FGF) receptor tyrosine kinase, epidermal growth factor (EGF) receptor tyrosine kinase, heparin-binding EGF-like growth factor (HB-EGF) receptor tyrosine kinase, platelet derived growth factor (PDGF) receptor tyrosine kinase, vascular endothelial growth factor (VEGF) receptor tyrosine kinase, nerve growth factor (VGF) receptor tyrosine kinase, hepatocyte growth factor (HGF) receptor tyrosine kinase, insulin receptor tyrosine kinase and insulin-like growth factor (IGF) receptor tyrosine kinase.

150 (New). The method according to claim 134, wherein said patient in need is one in need of: (i) inhibition of angiogenesis; (ii) inhibition of vascular smooth muscle cell

proliferation in disorders selected from the group consisting of atherosclerosis, hyperthrophic heart failure and postsurgical restenosis; (iii) inhibition of cell proliferation and migration in the treatment of primary tumors and metastasis; (iv) treatment of nonmalignant tumors; (v) treatment of diabetic retinopathy, psoriasis, rheumatoid arthritis, retrolental fibroplasia, macular degeneration, hemangioma, arteriovenous malformation, hypertrophic scars, acne, scleroderma and autoimmune diseases; or (vi) treatment of bone and cartilage related disorders and inherited skeletal disorders selected from the group consisting of achondroplasia, dwarfism and craniosynostosis.

151 (New). The method according to claim 150, wherein said patient in need is one in need of inhibition of angiogenesis, and wherein said tetropyrrolic macrocycle is 5,10,15-tris[2,3,5,6-tetrafluorophenyl-4-(N-methyl-2-pyridylium]-21H,23H-corrole triiodide, administered in an amount sufficient to effect said inhibition.

152 (New). The method according to claim 150, wherein said patient in need is one in need of inhibition of vascular smooth muscle cell proliferation in postsurgical restenosis, and wherein said tetropyrrolic macrocycle is 5,10,15,20-tetrakis(N-methyl-4-pyridylium)-21H, 23H-porphine tetra-p-tosylate or

5,10,15,20-tetrakis[4-(N-methyl-2-pyridylium) 2,3,5,6tetrafluoro-phenyl]-21H,23H-porphine tetraiodide, administered in
an amount sufficient to effect said inhibition.

153 (New). The method according to claim 150, wherein said patient in need is one in need of inhibition of cell proliferation and migration in the treatment of primary tumors and metastasis, and wherein said tetropyrrolic macrocycle is 5,10,15-tris[2,3,5,6-tetrafluorophenyl-4- (N-methyl-2-pyridylium)]-21H,23H-corrole triiodide, administered in an amount sufficient to effect said inhibition.

154 (New). The method according to claim 150, wherein said patient in need is one in need of inhibition of FGFR-3 tyrosine kinase activity and treatment of achondroplasia, and wherein said tetropyrrolic macrocycle is 5-pentafluorophenyl-10,15,20-tris(N-methyl-4-pyridylium)-21H, 23H-porphine triiodide, administered in an amount sufficient to effect said inhibition.

155 (New). A method for inhibiting angiogenesis, comprising administering an inhibitor which is a tetrapyrrolic macrocycle selected from the group consisting of:

### (a) a 5,10,15,20-tetraaryl-porphyrin of the formula:

wherein  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$ , the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ ) alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ )

alkylammonium radicals, wherein at least two of said  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$  aryl radicals are positively charged, n is an integer from 2 to 4 and X is a pharmaceutically acceptable anion; and

# (b) 5,10,15-triaryl-corrole of the formula:

wherein Ar<sub>1</sub>, Ar<sub>2</sub>, and Ar<sub>3</sub>, the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> alkylamino, amino-(C<sub>1</sub>-C<sub>8</sub>) alkylamino, and tri-(C<sub>1</sub>-C<sub>8</sub>) alkylamino radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl,

thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$  alkylammonium radicals, and wherein at least two of said  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$  aryl radicals are positively charged, n is an integer from 2 to 3 and X is a pharmaceutically acceptable anion; in an amount sufficient to inhibit angiogenesis.

156 (New). A method for prevention of restenosis after percutaneous transluminal coronary angioplasty, comprising administering an inhibitor which is a tetrapyrrolic macrocycle selected from the group consisting of:

(a) a 5,10,15,20-tetraaryl-porphyrin of the formula:

wherein  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$ , the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed

carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ ) alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8$ ) alkylamino, and tri- $(C_1$ - $C_8$ ) alkylammonium radicals, wherein at least two of said  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$  aryl radicals are positively charged, n is an integer from 2 to 4 and X is a pharmaceutically acceptable anion; and

### (b) 5,10,15-triaryl-corrole of the formula:

$$\begin{bmatrix} Ar_1 \\ N \\ N \\ H \end{bmatrix} + n$$

$$Ar_2 \\ H \\ N \\ HN$$

$$AR_2 \\ (X)_2$$

wherein  $Ar_1$ ,  $Ar_2$ , and  $Ar_3$ , the same or different, are each an aryl radical selected from the group consisting of a

carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> alkylamino, amino-(C<sub>1</sub>-C<sub>8</sub>) alkylamino, and tri-(C<sub>1</sub>-C<sub>8</sub>) alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> alkylamino, amino-(C<sub>1</sub>-C<sub>9</sub>) alkylamino, and tri-(C<sub>1</sub>-C<sub>8</sub>) alkylammonium radicals, and wherein at least two of said Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub> aryl radicals are positively charged, n is an integer from 2 to 3 and X is a pharmaceutically acceptable anion;

in an amount sufficient to inhibit smooth muscle cell proliferation.

157 (New). A method for inhibition of vascular smooth muscle cell proliferation in disorders selected from the group consisting of atherosclerosis, hyperthrophic heart failure and postsurgical restenosis, comprising the administration of an

inhibitor which is a tetrapyrrolic macrocycle selected from the group consisting of:

(a) a 5,10,15,20-tetraaryl-porphyrin of the formula:

wherein Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub>, the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> alkylamino, amino-(C<sub>1</sub>-C<sub>8</sub>) alkylamino, and tri-(C<sub>1</sub>-C<sub>8</sub>) alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub>

alkoxy,  $C_1$ - $C_8$  alkylamino, amino- $(C_1$ - $C_8)$  alkylamino, and tri- $(C_1$ - $C_8)$  alkylammonium radicals, wherein at least two of said  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$  aryl radicals are positively charged, n is an integer from 2 to 4 and X is a pharmaceutically acceptable anion; and

(b) 5,10,15-triaryl-corrole of the formula:

in an amount sufficient to inhibit said vascular smooth muscle cell proliferation.

158 (New). A 5,10,15,20-tetraaryl-porphyrin of the formula:

Page 22 of 33

wherein Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub>, the same or different, are each an aryl radical selected from the group consisting of a carboaryl, a heteroaryl and a mixed carboaryl-heteroaryl radical, wherein said carboaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of phenyl, biphenyl and naphthyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy,  $C_1-C_8$  alkylamino, amino- $(C_1-C_8)$  alkylamino, and tri- $(C_1-C_8)$ alkylammonium radicals, and said heteroaryl radical by itself or as part of a mixed carboaryl-heteroaryl radical is selected from the group consisting of furyl, thienyl, pyrrolyl, imidazolyl, thiazolyl, pyridyl, pyrimidyl, and triazinyl substituted by one or more halogen atoms, and/or one or more C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkoxy,  $C_1-C_8$  alkylamino, amino- $(C_1-C_8)$  alkylamino, and tri- $(C_1-C_8)$ alkylammonium radicals, wherein at least two of said  $Ar_1$ ,  $Ar_2$ , Ar<sub>3</sub>, and Ar<sub>4</sub> aryl radicals are positively charged, n is an integer from 2 to 4 and X is a pharmaceutically acceptable anion, provided that at least two of said at least two positively charged Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub> aryl radicals are selected from the group consisting of N- $(C_1-C_8)$  alkyl-pyridylium, 4-tri $(C_1-C_8)$  alkylammonium) -2,3,5,6-tetrafluorophenyl and  $4-N-(C_1-C_8)$  alkylpyridylium) -2,3,5,6-tetrafluorophenyl and, when at least two of said positively charged Ar<sub>1</sub>, Ar<sub>2</sub>, Ar<sub>3</sub>, and Ar<sub>4</sub> radicals are N-

 $(C_1-C_8)$  alkyl- pyridylium, at least one of the remaining  $Ar_1$ ,  $Ar_2$ ,  $Ar_3$ , and  $Ar_4$  is a non-positively charged aryl radical selected from pentafluorophenyl or 4-amino( $C_1-C_8$ ) alkylamino-2,3,5,6-tetrafluorophenyl.

159 (New). The porphyrin of claim 158 being selected from the group consisting of the compounds 5-pentafluorophenyl10,15,20-tris(N-methyl-4-pyridylium)-21H, 23H-porphine triiodide
[P16]; 5,15-bis(pentafluorophenyl)-10,20-bis(N-methyl-4pyridylium)-21H, 23H- porphine diiodide [P17]; 5,10-bis (pentafluorophenyl)-15, 20-bis(N-methyl-4-pyridylium)-21H, 23H-porphine
diiodide [P18]; 5,10,15-tris(N-methyl-4-pyridylium)-20-(2,3,5,6tetrafluoro-4-aminopropyl-amino-phenyl)-21H,23H-porphine
triiodide [P19] and 5,10,15,20-tetrakis[4-(N-methyl-2pyridylium)-2,3,5,6-tetrafluoro-phenyl]-21H, 23H-porphine
tetraiodide [P20].